

Applicant : Huy A. Bui  
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Attorney's Docket No.: 12671-035001

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Original) A method of calibrating an ion source, the ion source including a sample control system including a sample holder for supporting a sample plate in a sample plane and a laser source having a focal point representing a point at which a beam generated by the laser source intersects the sample plane, the method comprising:

mounting a sample plate in the sample holder, the sample plate including one or more target regions;

determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system, the relationship being determined at least in part by aligning one or more fiducials relative to a reference point of the sample control system, the fiducials defining reference points of the sample plate coordinate system; and

using the determined relationship to align a target region of the sample plate with ion optics of a mass spectrometer for a mass spectrometric analysis.

2. (Original) The method of claim 1, wherein at least one of the fiducials is positioned at a known displacement from a target location of at least one of the target regions.

3. (Original) The method of claim 2, wherein at least one of the one or more fiducials is formed on a surface of the sample plate.

4. (Original) The method of claim 2, wherein:

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at least one of the one or more fiducials is formed on a surface of the sample holder.

5. (Original) The method of claim 2, wherein:  
the target location of at least one of the target regions is a centroid of the at least one of the target regions.

6. (Original) The method of claim 2, wherein:  
the at least one of the fiducials forms the target location of the at least one of the target regions.

7. (Original) The method of claim 1, wherein the one or more fiducials include a first fiducial and a second fiducial disposed at a known displacement from the first fiducial, and determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system includes:

aligning the reference point with a first fiducial of the one or more fiducials;

moving the sample plate relative to the sample control system or the focal point by a distance and in a direction corresponding to the known displacement; and

determining an alignment error of the coordinate systems of the sample control system and the sample plate based at least in part on the aligning and the moving.

8. (Original) The method of claim 1, wherein determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system includes:

generating a first image of the sample plate, the first image including a representation of at least a first fiducial of the one or more fiducials;

processing the first image to identify a location of the first fiducial in the first image;

aligning the reference point of the sample control system relative to the identified location of the first fiducial; and

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determining an alignment error of the coordinate systems of the sample control system and the sample plate based at least in part on the alignment of the reference point relative to the identified location of the first fiducial.

9. (Original) The method of claim 8, wherein determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system includes:

processing the first image to identify a location of a second fiducial in the first image;  
aligning the reference point of the sample control system relative to the identified location of the second fiducial; and

determining an alignment error of the coordinate systems of the sample control system and the sample plate based at least in part on the alignment of the reference point relative to the identified location of the second fiducial.

10. (Original) The method of claim 9, wherein determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system includes:

moving the sample plate relative to the reference point;  
generating a second image of the sample plate, the second image including a representation of a third fiducial of the one or more fiducials;  
processing the second image to identify a location of a third fiducial in the second image;  
aligning the reference point of the sample control system relative to the identified location of the third fiducial; and

determining an alignment error of the coordinate systems of the sample control system and the sample plate based at least in part on the alignment of the reference point relative to the identified location of the third fiducial.

11. (Original) The method of any of claims 1, 7, 8, 9 and 10, wherein:

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the processing, aligning, or determining an alignment error are performed automatically in a sample control application.

12. (Original) The method of claim 1, further comprising:  
calibrating the focal point of the laser source and the coordinate system of the sample control system.
13. (Original) The method of claim 12, wherein:  
calibrating the focal point of the laser source and the coordinate system of the sample control system includes aligning the focal point of the laser source and the reference point of the sample control system with the ion optics.
14. (Original) The method of claim 13, wherein aligning the focal point of the laser source and the reference point of the sample control system with the ion optics includes:  
identifying a point in the sample plane corresponding to a center axis of the ion optics;  
and  
aligning the focal point of the laser source and the reference point of the sample control system with the identified point.
15. (Original) The method of claim 12, wherein aligning the focal point of the laser source and the reference point of the sample control system with the ion optics includes:  
aligning the reference point of the sample control system with a central axis of the ion optics; and  
aligning the focal point with the reference point of the sample control system.
16. (Original) The method of claim 1, wherein determining a relationship includes:  
determining one or more offsets that relate the coordinate system of the sample plate and the coordinate system of the sample control system.

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17. (Original) The method of claim 16, wherein using the determined relationship includes:

using the offsets to control a movement of the sample plate relative to the focal point or a firing of the laser source, with an accuracy of less than about  $\pm 100 \mu\text{m}$ .

18. (Original) The method of claim 1, wherein:

one or more of the fiducials includes two lines arranged in substantially orthogonal configuration.

19. (Original) A sample plate for use in a MALDI ion source of a mass spectrometer, comprising:

a first surface;

one or more target regions supported in or on the first surface, the target regions being configured to receive a sample including an analyte disposed in a matrix material; and

one or more fiducials arranged on the first surface, the fiducials being formed independently of the one or more target regions, one or more of the fiducials being located a predetermined distance in a predetermined direction from a target location of one or more of the target regions, such that the fiducials are usable in an at least partially automated process for aligning the sample plate in an ion source of a mass spectrometer.

20. (Original) A computer program product, tangibly embodied on a computer-readable medium, for calibrating an ion source, the ion source including a sample control system including a sample holder for supporting a sample plate in a sample plane and a laser source having a focal point representing a point at which a beam generated by the laser source intersects the sample plane, the product including instructions operable to cause data processing apparatus to perform operations comprising:

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receiving data indicating that a sample plate is mounted in the sample holder, the sample plate including one or more target regions;

determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system, the relationship being determined at least in part by aligning one or more fiducials relative to a reference point of the sample control system, the fiducials defining reference points of the sample plate coordinate system; and

using the determined relationship to align a target region of the sample plate with ion optics of a mass spectrometer for a mass spectrometric analysis.

21. (Original) The computer program product of claim 20, wherein at least one of the fiducials is positioned at a known displacement from a target location of at least one of the target regions.

22. (Original) The computer program product of claim 21, wherein at least one of the one or more fiducials is formed on a surface of the sample plate.

23. (Original) The computer program product of claim 21, wherein:  
at least one of the one or more fiducials is formed on a surface of the sample holder.

24. (Original) The computer program product of claim 21, wherein:  
the target location of at least one of the target regions is a centroid of the at least one of the target regions.

25. (Original) The computer program product of claim 21, wherein:  
the at least one of the fiducials forms the target location of the at least one of the target regions.

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26. (Original) The method of claim 20, wherein the one or more fiducials include a first fiducial and a second fiducial disposed at a known displacement from the first fiducial, and determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system includes:

- aligning the reference point with a first fiducial of the one or more fiducials;
- moving the sample plate relative to the sample control system or the focal point by a distance and in a direction corresponding to the known displacement; and
- determining an alignment error of the coordinate systems of the sample control system and the sample plate based at least in part on the aligning and the moving.

27. (Original) The computer program product of claim 20, wherein determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system includes:

- generating a first image of the sample plate, the first image including a representation of at least a first fiducial of the one or more fiducials;
- processing the first image to identify a location of the first fiducial in the first image;
- aligning the reference point of the sample control system relative to the identified location of the first fiducial; and
- determining an alignment error of the coordinate systems of the sample control system and the sample plate based at least in part on the alignment of the reference point relative to the identified location of the first fiducial.

28. (Original) The computer program product of claim 27, wherein determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system includes:

- processing the first image to identify a location of a second fiducial in the first image;
- aligning the reference point of the sample control system relative to the identified location of the second fiducial; and

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determining an alignment error of the coordinate systems of the sample control system and the sample plate based at least in part on the alignment of the reference point relative to the identified location of the second fiducial.

29. (Original) The computer program product of claim 28, wherein determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system includes:

- moving the sample plate relative to the reference point;
- generating a second image of the sample plate, the second image including a representation of a third fiducial of the one or more fiducials;
- processing the second image to identify a location of a third fiducial in the second image;
- aligning the reference point of the sample control system relative to the identified location of the third fiducial; and

determining an alignment error of the coordinate systems of the sample control system and the sample plate based at least in part on the alignment of the reference point relative to the identified location of the third fiducial.

30. (Original) The computer program product of any of claims 20, 26, 27, 28 and 29, wherein:

the processing, aligning, or determining an alignment error are performed automatically in a sample control application.

31. (Original) The computer program product of claim 20, further comprising:  
calibrating the focal point of the laser source and the coordinate system of the sample control system.

32. (Original) The computer program product of claim 31, wherein:



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calibrating the focal point of the laser source and the coordinate system of the sample control system includes aligning the focal point of the laser source and the reference point of the sample control system with the ion optics.

33. (Original) The computer program product of claim 32, wherein aligning the focal point of the laser source and the reference point of the sample control system with the ion optics includes:

identifying a point in the sample plane corresponding to a center axis of the ion optics;  
and

aligning the focal point of the laser source and the reference point of the sample control system with the identified point.

34. (Original) The computer program product of claim 31, wherein aligning the focal point of the laser source and the reference point of the sample control system with the ion optics includes:

aligning the reference point of the sample control system with a central axis of the ion optics; and

aligning the focal point with the reference point of the sample control system.

35. (Original) The computer program product of claim 20, wherein determining a relationship includes:

determining one or more offsets that relate the coordinate system of the sample plate and the coordinate system of the sample control system.

36. (Original) The computer program product of claim 35, wherein using the determined relationship includes:

using the offsets to control a movement of the sample plate relative to the focal point or a firing of the laser source, with an accuracy of less than about  $\pm 100 \mu\text{m}$ .

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37. (Original) The computer program product of claim 20, wherein:  
one or more of the fiducials includes two lines arranged in substantially orthogonal configuration.

38. (Original) A mass spectrometry system, comprising:  
an ion source, the ion source including a sample control system including a sample holder for supporting a sample plate in a sample plane and a laser source having a focal point representing a point at which a beam generated by the laser source intersects the sample plane;  
and

a processing unit configured to perform operations comprising:  
determining a relationship between a coordinate system of a sample plate mounted in the sample holder and a coordinate system of the sample control system, the relationship being determined at least in part by aligning one or more fiducials relative to a reference point of the sample control system, the fiducials defining reference points of the sample plate coordinate system; and  
using the determined relationship to align a target region of the sample plate with ion optics of a mass spectrometer for a mass spectrometric analysis.

39. (New) The method of claim 1, wherein:  
at least one of the fiducials is positioned at a determinable displacement from the target location of at least one of the target regions.

40. (New) The method of claim 39, wherein:  
at least one of the target regions provides at least one of the fiducials.

41. (New) The method of claim 40, wherein:  
a perimeter of at least one of the target regions provides at least one of the fiducials.

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42. (New) The method of claim 1, wherein:

at least one of the one or more target regions comprises a track of eluent.

43. (New) A method of generating ions for mass spectrometry, comprising:

depositing a sample onto a sample plate to provide one or more target regions in the sample;

mounting the sample plate in a sample holder of an ion source having a sample control system;

determining a relationship between a coordinate system of the sample plate and a coordinate system of the sample control system, the relationship being determined at least in part by aligning one or more fiducials relative to a reference point of the sample control system, the fiducials defining reference points of the sample plate coordinate system;

using the determined relationship to align a target region of the sample plate with ion optics of a mass spectrometer;

directing a beam from a laser source to a target location in the sample and at a known or determinable displacement from at least one of the fiducials.

44. (New) The method of claim 43, wherein:

the ion source comprises a matrix assisted laser desorption ionization (MALDI) source.

45. (New) The method of claim 43, wherein:

depositing the sample includes depositing eluent from a high pressure liquid chromatograph (HPLC).

46. The method of claim 45, wherein:

depositing the sample includes depositing the eluent in a track.